Race, Cardiovascular Reactivity, and Preterm Delivery Among Active-Duty Military Women

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Background: Rates of preterm delivery in the United States are higher in black women compared with whites. In this study, we examined cardiovascular reactivity and risk of preterm delivery among black and white military women.

Methods: We recruited a total of 500 black and white active-duty military women from the prenatal clinic at a large military installation, interviewing them early in pregnancy and again at 28 weeks of gestation. A subgroup of women underwent a computerized stress test to determine cardiovascular reactivity assessed as increases in heart rate and blood pressure compared with measurements taken before the stress test.

Results: Despite a relatively low overall risk of preterm delivery (8.2%), we found the same 2-fold racial disparity reported in other populations (hazard ratio for preterm delivery in black women vs whites = 2.30; 95% confidence interval = 1.24–4.27). The disparity is present in all military ranks and is largest for medically indicated preterm deliveries. Among the 313 subjects who participated in the computerized stress testing, blacks exhibited more cardiac reactivity than whites. In black subjects only, a 1-mm increase in diastolic blood pressure reactivity was associated with 1.1 a day earlier delivery (−0.17 weeks). A similar trend was seen with heart rate.

Conclusions: Autonomic dysfunction after exposure to stressors may play a role in the timing of delivery among black women.

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The disparity in rates of preterm delivery between black and white women in the United States[1] is striking, seemingly intractable and not easily explained. Many of the suspected social and biologic differences between black and white women have been studied but seem to account for very little of the difference in rates of preterm delivery.[2] Among the explanations that have been proposed are that black women are subjected to more stressors[3,4] and are more susceptible to these stressors at the physiological level.[5]

One indicator of susceptibility to stressors is cardiovascular reactivity, which is defined as the propensity for an individual to undergo changes in blood pressure and heart rate during exposure to a stressor.[6] Higher levels of cardiovascular reactivity have been reported among black men and women.[7–9] Hemodynamic reactivity is presumed to be mediated by the neuroendocrine system, in particular norepinephrine.[10] In theory, alterations in maternal cardiovascular functioning coincident with changes in endocrine activity could lead to adverse pregnancy outcome.[11] Also, autonomic dysregulation may be associated with pregnancy complications that increase risk of preterm delivery.[12]

Two recent studies have examined the influence of cardiovascular reactivity on gestational age at delivery.[13,14] McCubbin and colleagues in Kentucky[13] found that in a sample of 40 primigravid women from a university prenatal clinic, diastolic blood pressure reactivity to a cognitive challenge (an interactive arithmetic task) was inversely related to both gestational age and birth weight; Pearson correlation coefficients were $r = -0.44$ and -0.39, respectively. Each millimeter of mercury increase in diastolic blood pressure was associated with a 0.31-week decrease in gestation at delivery. Systolic blood pressure and heart rate showed more modest correlations in the same direction. A study of 70 healthy pregnant women in Argentina[14] found that vascular reactivity (specifically, diastolic blood pressure increase) as assessed by the cold pressor test (immersing the subject's hand in cold water) also showed a negative correlation with gestational age ($r = -0.57$). Each mean millimeter of mercury increase in reactivity was associated with a 0.07-week decrease in gestational age at delivery.

We examined cardiovascular reactivity measured after mental challenge and the risk of preterm delivery in black military women as compared with their white counterparts.

METHODS

Subjects

This report focuses on 500 pregnant active-duty military women attending the prenatal clinic at a large military medical center during the years 1997–2000. Among 804 women who met entry criteria, 41 women refused to participate, leaving a total of 724 (94%). Eighty women had miscarriages and were excluded from the sample, and 63

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participants left the military base before delivery and were considered lost to follow up. We excluded 120 women of other races, leaving a sample for analysis of 130 black and 370 white subjects. Participants were interviewed at the time of enrollment early in pregnancy (6–12 weeks of gestation) and were asked to return at 28 weeks of gestation to fill out a second questionnaire and complete the psychophysiological testing to determine cardiovascular reactivity. The study protocol was approved by the relevant Institutional Review Boards. All participants gave signed informed consent.

Data Collection

The study questionnaire covered the following areas: sociodemographics (baseline); medical history (baseline); reproductive history (baseline); pregnancy complications (28 weeks); lifestyle factors (28 weeks); hours worked, job characteristics, and job stress (baseline and 28 weeks)[15]; and a measure of life stress (28 weeks).[16]

The psychophysiological testing session consisted of 2 standard 5-minute computer-controlled laboratory stressors: a mental arithmetic task and the Stroop color word-matching task.[17,18] In the arithmetic task, subjects were presented with a 4-digit number on the computer monitor and were instructed to subtract serially by 7s. At 1-minute intervals, subjects received verbal prompts (eg, "please subtract faster"). In the Stroop Color-Word task, subjects were presented with color names in colors that were either congruent or incongruent with the names. The task was to press the key corresponding to the color of the letters. The task was paced by the computer and a wrong response or failure to respond rapidly enough resulted in a message indicating "incorrect" on the screen. These standard laboratory stressors have been used previously with pregnant women.[13,19] Continuous blood pressure and heart rate responses were measured during a 5-minute seated baseline period and during the 5-minute recovery period after each task by means of a Finapres blood pressure cuff on the middle finger of the nondominant hand.[20]

Key Variables

Five job stress measures were created based on subscales of the NIOSH Job Stress Questionnaire[15]: workload, job control, role conflict, skill utilization, and job satisfaction. A more generalized measure of stress was based on Cohen's Perceived Stress Scale.[16] We also examined hours worked per week (40 or less vs more than 40).

Medical data on the course and outcome of the pregnancy were abstracted from the hospital records. Gestational age was based on the due date estimated by ultrasound measurements before 20 weeks of gestation. Physician's assessment of gestation at delivery reported in the medical record was used for 9 women with missing data on ultrasound and 14 women whose due date based on ultrasound differed by more than 30 days from the physician's assessment. Preterm delivery was defined as delivery after 20 and before 37 completed weeks of gestation.

Cardiovascular reactivity was assessed using change scores unless there was a dependence of the change score on the measurement taken before the stress test in which case residualized scores were used.[21] Measures calculated as the mean of the 2 task levels minus the baseline (prestress test) level were generated for heart rate, systolic blood pressure (SBP), and diastolic blood pressure (DBP). The task levels were aggregated to increase reliability.[22]

Statistical Methods

In preliminary analyses, we calculated rates of preterm delivery by delivery subtype, race, and military rank. In addition, we estimated Kaplan-Meier survival curves by race for gestational age at delivery in weeks.

We used a Cox proportional hazards model to determine overall risk factors for preterm delivery in black women relative to whites. Hazard rates (HRs) and 95% confidence intervals (CIs) were computed. Five women who were induced preterm after having spontaneous rupture of membranes were considered to have had spontaneous events. Nonspontaneous preterm deliveries were censored at the time of delivery. Deliveries after 37 completed weeks of gestation were no longer at risk for "failure." Potential confounders related to stress, lifestyle, and medical/obstetric factors were added to the model one by one and retained in the final model if they modified the coefficient for black women by 10% or more.[23]

We examined mean reactivity scores by race. Multiple linear regression models were used to evaluate the association of reactivity scores and gestational age at delivery while controlling for potential confounders. Models were initially constructed for spontaneous deliveries (n = 248) and then repeated including all deliveries (n = 313). Covariates tested as potential confounders were race, previous preterm delivery, complications during pregnancy, education, marital status, maternal age, body mass index, pregnancy weight gain, physical activity, smoking, coffee consumption, infant sex, and gestational age at time of testing. An interaction term for race was included to examine whether black women had higher levels of reactivity and, thus, potentially, a larger

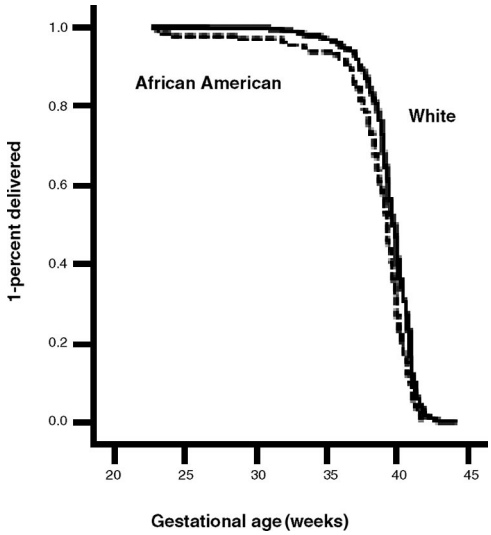

FIGURE 1. Kaplan-Meier survival curves showing the percent undelivered by week of gestation for black and white women.

TABLE 1. Hazard Ratios for Risk of Preterm Delivery Among Black Women Compared With White Women (n = 500)

Hazard Ratios	Spontaneous Deliveries HR (95% CI)	All Deliveries HR (95% CI)
Unadjusted	1.96 (0.95 to 4.08)	2.30 (1.24 to 4.27)
Adjusted for demographic and obstetric risk factors*	1.78 (0.82 to 3.83)	2.33 (1.22 to 4.44)
Further adjusted for work stressors and perceived stress†	1.81 (0.80 to 4.06)	2.17 (1.10 to 4.28)
Further adjusted for lifestyle variables‡	1.85 (0.81 to 4.24)	2.21 (1.11 to 4.44)

*Adjusted for maternal age, education, marital status, previous preterm delivery, parity, and complications during pregnancy.
†Adjusted for job control, job satisfaction, quantitative workload, skill utilization, role conflict, worked greater than 40 h per week, and perceived stress in addition to the variables listed.
‡Adjusted for smoking, coffee drinking, exercise during pregnancy, in addition to all variables listed.

impact on gestational age at delivery. We also performed linear regression analyses stratified by race.

RESULTS

The risk of preterm delivery in the total sample was 8.2% (n = 41). The risk was 5.2% for spontaneous preterm deliveries, 2.0% for medically indicated deliveries, and 1.0% for unknown type of labor.

The risk of preterm delivery among black women in this military population was approximately double that in white women (13.9% vs 6.2%) both for spontaneous preterm delivery (7.7% for black women compared with 4.3% for whites) and for medically indicated deliveries (3.8% compared with 1.4%). The difference by race was also present within military ranks (spontaneous preterm delivery rate, officers: black 8.3%, white 5.4%; higher enlisted: black 9.7%, white 4.9%; lower enlisted: black 8.7%, white 4.3%).

The Kaplan-Meier curve in Figure 1 shows the difference in gestational age at delivery between black mothers and white mothers ($P = 0.008$, Breslow test). The difference in percent delivered begins at 24 weeks. The maximum difference occurs around 33 weeks of gestation, but the difference is present throughout the preterm period.

Hazard ratios for preterm delivery among black women compared with white women show an approximately 2-fold difference in risk (for spontaneous deliveries: HR = 1.96; 95% CI = 0.95–4.08) (Table 1). The racial disparity is somewhat greater in the category "all deliveries," which includes those involving medical intervention (2.30; 1.24–4.27). Adjustment for a wide range of covariates led to some attenuation in the hazard ratios for spontaneous delivery; for all deliveries, the adjusted HRs were essentially unchanged. All analyses were rerun omitting the term for prior preterm delivery; because the results remained the same, we retained the model that includes this adjustment.

Stress Test Group

Only 313 subjects agreed to the psychophysiological testing (stress test group). Of the women who refused, most said it was because of the time involved (n = 97). Others failed to show for a scheduled appointment (n = 27), and in some instances, the computer malfunctioned during the testing session (n = 27). Remaining losses were due to miscellaneous reasons.

Women who took the stress test were similar to those who did not in many respects, including age, education, military rank, pregnancy complications, and perceived stress. However, an important difference was that the nontest takers had a substantially higher risk of preterm delivery than the test takers (10.1% vs 6.6%). They also were different with respect to job stressors; the nontest takers were more likely to report low job control (66% vs 49%) and low job satisfaction

TABLE 2. Mean Baseline Blood Pressure, Baseline Heart Rate, and Stress Reactivity Change Scores

	Spontaneous Deliveries				All Deliveries			
	Black (n = 58)		White (n = 190)		Black (n = 75)		White (n = 238)	
	Mean	(SE)	Mean	(SE)	Mean	(SE)	Mean	(SE)
Heart rate (beats/min)	87.3	(1.3)	85.0	(0.7)	87.7	(1.1)	85.2	(0.6)
Systolic blood pressure (mm Hg)	106.5	(1.7)	108.6	(0.8)	108.1	(1.6)	108.5	(0.8)
Diastolic blood pressure (mm Hg)	61.5	(1.1)	60.0	(0.6)	60.9	(1.1)	58.6	(0.6)
Heart rate change (beats/min)	3.1	(0.4)	3.4	(0.3)	3.1	(0.4)	3.3	(0.3)
Systolic blood pressure change (mm Hg)	8.8	(1.2)	6.3	(0.6)	9.2	(1.0)	6.5	(0.5)
Diastolic blood pressure change (mm Hg)	4.3	(0.6)	3.8	(0.3)	4.8	(0.5)	3.9	(0.3)

SE indicates standard error.

(64% vs 47%) and were less likely to report a high workload (35% vs 46%). The nontest takers were also somewhat more likely to be black (29% vs 24%). As a result of the nontest takers' higher risk of preterm delivery, the group undergoing psychophysiological testing showed no overall difference by race in risk of spontaneous preterm delivery, although medically indicated deliveries did differ by race.

Table 2, based on data from the stress test group, compares measurements taken before the stress test and mean reactivity by race for the 3 cardiovascular parameters: SBP, DBP, and heart rate. Black women had a slightly higher mean heart rate and DBP before the stress test. Levels of SBP and DBP reactivity were higher in the all-deliveries category compared with the spontaneous-delivery category. Compared with whites, blacks showed higher SBP reactivity among both spontaneous deliveries and all deliveries. Among all deliveries, DBP reactivity was higher in blacks. Table 3 presents results of the race-stratified multiple regression analyses of reactivity and gestational age at delivery (in weeks). Associations for blacks are stronger in the all-deliveries analyses. Among all deliveries, a 1-mm Hg increase in DBP reactivity was associated with a reduction in gestational age of 0.17 weeks (95% CI = −0.27 to −0.06), or 1.1 days. An association similar in magnitude was observed for increased heart rate. SBP reactivity showed a modest association with gestational age among black women in both delivery categories. There were no notable associations between reactivity and gestational age among white women. Interaction terms with race were examined; substantial variability was found among all deliveries for DBP reactivity ($P = 0.002$) and heart rate reactivity ($P = 0.004$).

DISCUSSION

Despite a relatively low overall risk of preterm delivery (8.2%), the risk of white (6.2%) and black (13.9%) active-duty military women from the same Air Force facility showed a more than 2-fold difference. The only previous study of racial disparity in pregnant military women, by Adams et al,[24] also found an excess risk of preterm delivery for black women relative to white women, with the association being stronger for medically indicated preterm deliveries and for deliveries before 33 weeks, as in our study.

Blacks have been found to have greater reactivity to stressors than whites, particularly in the vasculature, and theory has predicted that this greater reactivity may underlie their increased risk for hypertension.[7,8] Hyperreactivity might also be implicated in preterm delivery either directly or indirectly through hypertensive disorders of pregnancy.[12]

Like the 2 previous studies of pregnant women in Kentucky[13] and Argentina,[14] we observed an association between increased reactivity and gestational age at delivery. In our study, the association was restricted to the subgroup of black women. The study in Kentucky[13] found a marginally significant interaction between diastolic reactivity and maternal race with the results suggesting a stronger association in blacks. As in both of the previous studies, the association we found was primarily with diastolic blood pressure. The observed decrease of 0.17 weeks' gestation with a 1-mm Hg increase in DBP is less than

TABLE 3. Adjusted Gestational Age Differences (weeks) Associated With Stress Reactivity*: Stress Test Subgroup

	Spontaneous Deliveries			All Deliveries		
	All Subjects (n = 248) Adjusted Difference (95% CI)	Black (n = 58) Adjusted Difference (95% CI)	White (n = 190) Adjusted Difference (95% CI)	All Subjects (n = 313) Adjusted Difference (95% CI)	Black (n = 75) Adjusted Difference (95% CI)	White (n = 238) Adjusted Difference (95% CI)
Systolic blood pressure (mm Hg)	−0.02 (−0.0 to 0)	−0.04† (−0.08 to 0.01)	−0.02 (−0.05 to 0.01)	−0.03 (−0.05 to 0)	−0.06† (−0.10 to 0)	−0.02 (−0.05 to 0.01)
Diastolic blood pressure (mm Hg)	−0.004‡ (−0.05 to 0.05)	−0.09† (−0.18 to 0)	−0.003†‡ (−0.05 to 0.06)	−0.04‡ (−0.08 to 0)	−0.17† (−0.27 to 0.06)	0.002†‡ (−0.05 to 0.05)
Heart rate (beats/min)§	0.09‡ (−0.11 to 0.28)	−0.21‡ (−0.65 to 0.24)	0.20‡ (−0.07 to 0.48)	0.10‡ (−0.07 to 0.27)	−0.25‡ (−0.63 to 0.14)	0.22‡ (−0.01 to 0.46)

All models adjusted for maternal age, race, education, marital status, parity, previous preterm delivery, and complications during pregnancy.
*Change in gestational age for 1-mm increase from baseline in systolic or diastolic BP or for an increase of 1 beat/min of heart rate.
†Also adjusted for the variable of worked >40 h/wk.
‡Also adjusted for the infertility variable.
§Mean heart rate increase is adjusted to take into account correlation between baseline heart rate and heart rate increase.

the 0.31 weeks observed by McCubbin[13] and more than the 0.07 weeks reported by the Argentinian group.[14]

In our data, the association of blood pressure reactivity with gestational age at delivery, although modest, is twice as large among all deliveries as among spontaneous deliveries. This is consistent with reactivity being a mediating mechanism for certain pregnancy complications that lead to medical intervention.

Our study has limitations that should be considered. The results for reactivity are based on the approximately two thirds of subjects who participated in the psychophysiological testing; however, this is a participation rate not unlike that for the onerous component of many other studies. The nontest takers had greater exposure to sources of job stress and a higher rate of preterm delivery. This loss reduced sample size and might have introduced a selection bias. Although we observed an association between reactivity and gestational age among black women, we cannot evaluate whether this reactivity may have contributed to the black/white disparity in risk of preterm delivery. This is because in the stress test group, the percent delivering preterm among the black women was fairly similar to that among the whites, reflecting the higher risk of preterm delivery in the nontest takers.

In addition, we were unable to ascertain pregnancy outcomes for 63 subjects who left the military base before delivery. It is difficult to imagine that this would be a biased subset, however, because their relocation was determined by military considerations. Finally, an underlying assumption is that reactivity to laboratory stressors correlates with reactivity to real life stressors, a point on which there is little evidence, although the best designed studies are supportive.[11]

In conclusion, we observed a 2-fold racial difference in preterm delivery in a population of active-duty military women, a difference that was present within groups stratified by rank and a difference we were unable to explain. Nevertheless, our results with respect to cardiovascular reactivity to stressors suggest a promising direction. Reactivity levels in our study were higher among black women than whites and, in the subgroup of black women, reactivity in diastolic blood pressure showed an inverse correlation with gestational age at delivery. Our data suggest that among black women, cardiac reactivity may contribute to the risk of earlier delivery.

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